Response of Thyroid Functional Tissue Units to Space-Like Radiation Fields

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Abstract:

The thyroid like most epithelial-based glandular tissues are a common site of tumor development and sensitive to ionizing radiation induced carcinogenic changes. Using thyroid as a model, especially the well-defined normal cell line that we have characterized, provides us the opportunity to investigate how normal tissue responds to ionizing radiation from different sources, doses and dose rates, at multiple levels. From "Radiation Hazards to Crews of Interplanetary Missions" a major question raised was "Are there studies that can be conducted to increase the confidence of extrapolation from rodents to humans of radiation-induced genetic alterations that in turn could enhance similar extrapolations for cancer?" We have established tissue analog produced during growth in a low-shear bioreactor is a realistic three-dimensional replica of the tissue being modeled. The bioreactor system provides stable environmental controls not achievable by other methods. Objective-Confirm and extend the characteristic pattern of radiation modulated gene expression in rat thyroid tissue analogs using space-like low dose/low dose rate radiation, and challenge the chronically irradiated analogs with an acute 2Gy dose of proton radiation. We hypothesize that a low-dose/low-dose rate "priming" exposure to radiation will invoke a suite of cell and tissue level homeostatic mechanisms that will be reflected by gene expression profiles and complementary structural and functional changes in component cells and their functional tissue units (FTU's, i.e. follicles). The principal regulatory elements in the priming transition will be transforming growth factor-beta (TGF-b) and protein kinase C isoforms (pkc). These will steer other respondent genes that will be identified by microarray expression profiling. It is expected that the transcription factor AP-1 and accessory oncogenes and cell coordinating gene products will exhibit the most significant alterations.